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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Nicolaides *et al.*

Confirmation No.: 5193

Serial No.: 09/912,697

Group Art Unit: 1648

Filing Date: July 25, 2001

Examiner: Z. Lucas

For: METHODS FOR GENERATING ANTIBIOTIC RESISTANT MICROBES AND NOVEL ANTIBIOTICS

Express Mail No. **EV 160094365 US**
Date of Deposit: December 4, 2002

Assistant Commissioner for Patents
Washington D.C. 20231

Response to Requirement for Restriction

This is in response to the Official Action dated September 10, 2002. The fee for a two-month extension of time is included.

The Applicants appreciate the clarification of the "matrix-type restriction requirement" as explained to Felicity Groth, Esq. on October 4, 2002. In that telephonic discussion, the Examiner explained that the only election of species is the species of anthracene derivative. The other subdivisions of the Groups I and II are actually also Groups themselves. However, the Examiner indicated that subgroups of claims may be rejoined if the Examiner finds that the search is not unduly burdensome. This would appear to indicate that it is possible that subgroups A1-A3 could be collapsed into a single subgroup A, which could be rejoined with subgroups B and C into one group – Group I.

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In order to be fully responsive to the Office Action, Applicants hereby elect Group I (A)(A1) with traversal in part. Claims readable upon the elected group are Claims 1-3, 14-27 and 38. It is the Applicants understanding that the Examiner may rejoin subgroups A1-A3 should the search prove not to be unduly burdensome. Should this occur, Group I (A) (A3) will require another restriction. In that circumstance, Applicants hereby elect (i) an anthracene derivative as the subgroup, and 1,2-dimethylanthracene as the elected species, reserving the right to pursue the other species upon allowance of the generic claim.

Applicants traverse the Requirement for Restriction in part. That is, Applicants earnestly submit that subgroups A1-A3 should be rejoined into a single group A. The Examiner states that subgroups A1-A3 are unrelated as they are not disclosed as being capable of use together, and they have different modes of operation, different functions, or different effects. Applicants disagree. In each case, whether mismatch repair is inhibited through the use of a dominant negative allele of a mismatch repair gene, an antisense molecule directed against a mismatch repair gene, or a compound that blocks mismatch repair. These strategies could be used together. Moreover, the function of the compounds and effects are the same: mismatch repair is inhibited and the cells become hypermutable. The modes of operation are also similar, in that functional mismatch repair complexes are inhibited. It is not the same as a case in which different pathways are targeted to achieve the same result.

Furthermore, the Examiner has not presented any evidence that the subject matter of these claims has acquired a separate status in the art, or that subgroups A1-A3 would require a search of different classes or subclasses. As the Examiner has clearly failed to

demonstrate that a search of the subject matter would be unduly burdensome, Applicants respectfully submit that subgroups A1-A3 should be rejoined.

Should the Examiner agree to rejoin subgroups A1-A3, Applicants elect Group I (A), including subgroup (i) and 1,2-dimethylanthracene as the species. In this instance, the claims readable upon the elected species are claims 1-9, 14-29 and 38.

Applicants also urge the Examiner to reconsider the Requirement for Restriction with respect to subgroups A, B and C. Subgroups A, B and C are all drawn to generating antibiotic resistant bacteria using hypermutable bacteria. The bacteria may be hypermutable due to blocking mismatch repair activity, using bacteria with an endogenous defect in mismatch repair, or by overexpressing wild-type mismatch repair proteins in the bacteria (which has been shown to confer a dominant negative phenotype in bacteria). The function and the effects are the same: the cells are hypermutable and accumulate mutations in the genome leading to an antibiotic-resistant phenotype. The modes of operation of the method are the same: bacteria that are hypermutable are exposed to an antibiotic and resistant colonies are selected as the antibiotic resistant microbes.

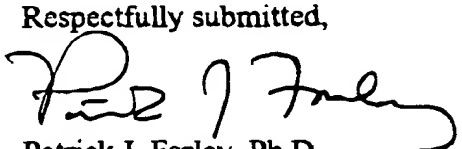
Again, the Examiner has presented no evidence that the subject matter of these claims has acquired a separate status in the art or that subgroups A, B and C would require a search of different classes or subclasses. As the Examiner has clearly failed to demonstrate that a search of the subject matter would be unduly burdensome, Applicants respectfully submit that subgroups A, B and C must be rejoined.

Again, should the Examiner agree to rejoin subgroups A, B and C, Applicants elect Group I, including subgroup (i) and 1,2-dimethylanthracene as the species. In this

instance, the claims readable upon the elected species include claims 1-9, 14-29 and 35-41.

Applicants respectfully request that the examiner reconsider the Requirement for Restriction and rejoin the groups as indicated above.

Respectfully submitted,



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